

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the claims:

1. (Presently Amended) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide **B-2036 of [SEQ. ID. NO. 1]** in genetically modified host cells, the process comprising the step of:
 - (a) contacting with said impurity under sufficient conditions a mercapto compound to decrease said amount of said impurity, wherein said impurity is a trisulfide isoform of said polypeptide.
2. (Presently Amended) The process of ~~embodiment~~ **claim 1** further comprising the step of:
 - (b) growing said host cells to produce said polypeptide, wherein said growing is conducted either before or during said contacting step (a).
3. (Presently Amended) The process of ~~embodiment~~ **claim 2** further comprising the step of:
 - (c) purifying said polypeptide to yield a purified polypeptide.
4. (Presently Amended) The process of ~~embodiment~~ **claim 3** further comprising the step of:
 - (d) pegylating said purified polypeptide.
5. (Presently Amended) The process of ~~embodiment~~ **claim 2** wherein said mercapto compound is selected from the group consisting of sulfites, glutathione, beta-mercaptoethanol, dithiothreitol, mercaptoethylamine, dithioerythritol, tris(2-carboxyethyl) phosphine hydrochloride, cysteine, and cysteine in combination with cystine.

6. (Presently Amended) The process of ~~embodiment~~ claim 1 wherein said mercapto compound is selected from the group consisting of sulfites, glutathione, beta-mercaptoethanol, dithiothreitol, mercaptoethylamine, dithioerythritol, tris(2-carboxyethyl) phosphine hydrochloride, cysteine, and cysteine in combination with cystine.
7. (Presently Amended) The process of ~~embodiment~~ claim 5 wherein said mercapto compound comprises cysteine or a combination of cysteine and cystine.
8. (Presently Amended) The process of ~~embodiment~~ claim 6 wherein said mercapto compound comprises cysteine or a combination of cysteine and cystine.
9. (Presently Amended) The process of ~~embodiment~~ claim 7 wherein in said contacting step (a), said trisulfide isoform is contacted with said cysteine or combination of cysteine and cystine for a period of time sufficient to decrease said amount of said trisulfide isoform by at least about 10%.
10. (Presently Amended) The process of ~~embodiment~~ claim 9 wherein said period of time is sufficient to decrease said amount of said trisulfide isoform by at least about 50%.
11. (Presently Amended) The process of ~~embodiment~~ claim 8 wherein in said contacting step (a), said trisulfide isoform is contacted with said cysteine for a period of time sufficient to decrease said amount of said trisulfide isoform by at least about 10%.
12. (Presently Amended) The process of ~~embodiment~~ claim 11 wherein said period of time is sufficient to decrease said amount of said trisulfide isoform by at least about 50%.
13. (Presently Amended) The process of ~~embodiment~~ claim 1 wherein said mercapto compound is provided in a buffer.
14. (Presently Amended) The process of ~~embodiment~~ claim 2 wherein said mercapto compound is provided in a buffer.

15. (Presently Amended) The process of ~~embodiment~~ claim 7 wherein said cysteine or combination of cysteine and cystine is provided in a buffer.
16. (Presently Amended) The process of ~~embodiment~~ claim 8 wherein said cysteine or combination of cysteine and cystine is provided in a buffer.
17. (Presently Amended) The process of ~~embodiment~~ claim 15 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.
18. (Presently Amended) The process of ~~embodiment~~ claim 16 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.
19. (Presently Amended) The process of ~~embodiment~~ claim 17 wherein said initial combined cysteine and cystine concentration is from about 0.1 mM to about 10 mM.
20. (Presently Amended) The process of ~~embodiment~~ claim 18 wherein said initial combined cysteine and cystine concentration is from about 0.1 mM to about 10 mM.
21. (Presently Amended) The process of ~~embodiment~~ claim 19 wherein said initial combined cysteine and cystine concentration is from about 1 mM to about 5 mM.
22. (Presently Amended) The process of ~~embodiment~~ claim 20 wherein said initial combined cysteine and cystine concentration is from about 1 mM to about 5 mM.
23. (Presently Amended) The process of ~~embodiment~~ claim 13 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
24. (Presently Amended) The process of ~~embodiment~~ claim 14 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.

25. (Presently Amended) The process of ~~embodiment~~ claim 15 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
26. (Presently Amended) The process of ~~embodiment~~ claim 16 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
27. (Presently Amended) The process of ~~embodiment~~ claim 23 wherein said buffer comprises Tris.
28. (Presently Amended) The process of ~~embodiment~~ claim 26 wherein said buffer comprises Tris.
29. (Presently Amended) The process of ~~embodiment~~ claim 25 wherein said buffer comprises Tris.
30. (Presently Amended) The process of ~~embodiment~~ claim 24 wherein said buffer comprises Tris.
31. (Presently Amended) The process of ~~embodiment~~ claim 29 wherein after said contacting step (a) said Tris buffer has a Tris concentration from about 1 mM to about 200 mM.
32. (Presently Amended) The process of ~~embodiment~~ claim 28 wherein after said contacting step (a) said Tris buffer has a Tris concentration from about 1 mM to about 200 mM.
33. (Presently Amended) The process of ~~embodiment~~ claim 31 wherein said Tris concentration is from about 10 mM to about 50 mM.

34. (Presently Amended) The process of ~~embodiment~~ claim 32 wherein said Tris concentration is from about 10 mM to about 50 mM.
35. (Presently Cancelled) The process of embodiment 1 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
36. (Presently Cancelled) The process of embodiment 2 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
37. (Presently Cancelled) The process of embodiment 25 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
38. (Presently Cancelled) The process of embodiment 26 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
39. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.
40. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.
41. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein said combination of cysteine and cystine in said buffer and said B-2036 before said contacting step (a) have a molar ratio of moles of combined cysteine and cystine to moles of B-2036 from about 0.5 to about 1000.
42. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein said combination of cysteine and cystine in said buffer and said B-2036 and before said contacting step (a) have a molar ratio of moles of combined cysteine and cystine to moles of B-2036 from about 0.5 to about 1000.

43. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein after said contacting step (a) said B-2036 in said buffer has a B-2036 concentration from about 0.1 mg/ml to about 30 mg/ml.
44. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein after said contacting step (a) said B-2036 in said buffer has a B-2036 concentration from about 0.1 mg/ml to about 30 mg/ml.
45. (Presently Amended) The process of ~~embodiment~~ claim 43 wherein said B-2036 concentration is from about 0.5 mg/ml to about 20 mg/ml.
46. (Presently Amended) The process of ~~embodiment~~ claim 44 wherein said B-2036 concentration is from about 0.5 mg/ml to about 20 mg/ml.
47. (Presently Amended) The ~~method~~ process of ~~embodiment~~ claim 45 wherein said B-2036 concentration is from about 1 mg/ml to about 10 mg/ml.
48. (Presently Amended) The ~~method~~ process of ~~embodiment~~ claim 46 wherein said B-2036 concentration is from about 1 mg/ml to about 10 mg/ml.
49. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein after said contacting step (a) said buffer has a pH from about 6 to about 9.
50. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein after said contacting step (a) said buffer has a pH from about 6 to about 9.
51. (Presently Amended) The process of ~~embodiment~~ claim 49 wherein said pH is from about 7.5 to about 8.5.
52. (Presently Amended) The process of ~~embodiment~~ claim 50 wherein said pH is from about 7.5 to about 8.5.

53. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein said buffer and said B-2036 are maintained at a temperature from about 0°C to about 25°C after said contacting step (a).
54. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein said buffer and said B-2036 are maintained at a temperature from about 0°C to about 25°C after said contacting step (a).
55. (Presently Amended) The process of ~~embodiment~~ claim 53 wherein said temperature is from about 2°C to about 8°C.
56. (Presently Amended) The process of ~~embodiment~~ claim 54 wherein said temperature is from about 2°C to about 8°C.
57. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein said contacting step (a) is conducted for a time of at least about 30 minutes.
58. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein said contacting step (a) is conducted for a time of at least about 30 minutes.
59. (Presently Amended) The process of ~~embodiment~~ claim 57 wherein said time is from about 1 hour to about 24 hours.
60. (Presently Amended) The process of ~~embodiment~~ claim 58 wherein said time is from about 1 hour to about 24 hours.
61. (Presently Amended) The process of ~~embodiment~~ claim 59 wherein said time is from about 1 hour to about 4 hours.
62. (Presently Amended) The process of ~~embodiment~~ claim 60 wherein said time is from about 1 hour to about 4 hours.

63. (Presently Amended) The process of ~~embodiment~~ claim 37 25 wherein after said contacting step (a) said B-2036 in said buffer has a volume from about 1 L to about 5000 L.
64. (Presently Amended) The process of ~~embodiment~~ claim 38 26 wherein after said contacting step (a) said B-2036 in said buffer has a volume from about 1 L to about 5000 L.
65. (Presently Amended) The process of ~~embodiment~~ claim 63 wherein said volume is from about 10 L to about 500 L.
66. (Presently Amended) The process of ~~embodiment~~ claim 64 wherein said volume is from about 10 L to about 500 L.
67. (Presently Amended) The process of ~~embodiment~~ claim 65 wherein said volume is from about 100 L to about 300 L.
68. (Presently Amended) The process of ~~embodiment~~ claim 66 wherein said volume is from about 100 L to about 300 L.
69. (Withdrawn) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:
- (a) contacting a chelating agent under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity,
- wherein said impurity is a trisulfide isoform of said polypeptide.
70. (Withdrawn) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

- (a) contacting a metal salt under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity, wherein said impurity is a trisulfide isoform of said polypeptide.

71. (Withdrawn) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

- (a) contacting a chelating agent under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity, wherein said impurity is a des-phe isoform of said polypeptide.

72. (Withdrawn) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

- (a) contacting a metal salt under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity, wherein said impurity is a des-phe isoform of said polypeptide.

73. (Withdrawn) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

- (a) contacting a chelating agent under sufficient conditions with (1) said impurity, (2) said growth hormone polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity, wherein said impurity is a des-phe isoform of said polypeptide.

74. (Withdrawn) A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

(a) contacting a metal salt under sufficient conditions with (1) said impurity, (2) said growth hormone polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity, wherein said impurity is a des-phe isoform of said polypeptide.

75. (Withdrawn) The process of embodiment 73, wherein said contacting step (a) is conducted in the absence of a mercapto compound.

76. (Withdrawn) The process of embodiment 74, wherein said contacting step (a) further comprises contacting with said metal salt in combination with a mercapto compound.